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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/860,844	09/29/97	WEININGER S	GP-100C1

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EXAMINER	
MARSCHEL,A	
ART UNIT	**PAPER NUMBER**
1631	17

DATE MAILED: 08/15/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/860,844	Weininger et al.
Examiner	**Group Art Unit**
Ardin Marschel	1631

☒ Responsive to communication(s) filed on *May 10, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *28, 29, and 49* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *28, 29, and 49* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

The art unit designated for this application has changed. Applicant(s) are hereby informed that future correspondence should be directed to Art Unit 1631.

Applicants' arguments, filed 5/10/00, have been fully considered and they are deemed to be persuasive to overcome rejections previously of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. However, upon reconsideration, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

If applicant desires priority under 35 U.S.C. § 120 or § 371 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of non-provisional application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Claims 28, 29, and 49 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for

failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 49, lines 1-6, the TBAs are described as "each optionally comprising a DNA recognition unit, assembly sequences,...". This phrase is reasonably interpreted as indicating that the TBAs may or may not (that is, optionally) contain (that is, comprise) a DNA recognition unit, etc. as listed in lines 1-6 of claim 49. Thus, some TBAs in the claimed method may not contain a DNA recognition unit. In line 6 of claim 49 the phrase "such that upon proximal binding via the DNA recognition unit of each component TBA..." indicates that each component TBA contains at least a DNA recognition unit. This conflicts with the phrase in line 4 of claim 49 where each component TBA "optionally" comprises a DNA recognition unit. That is, what claim practice is meant for lines 6-8 of claim 49 for component TBAs without a DNA recognition unit? Clarification via clearer claim wording is requested.

The metes and bounds of what is meant as to a target binding assembly (TBA) are vague and indefinite. The specification at page 5, lines 19-33, seems to indicate that TBAs bind to a (target binding region)TBR which is made up of a (probe nucleic acid)PNA and a (target nucleic acid)TNA in a PNA-TNA hybrid pair as given on page 5, lines 21-22. Using this interpretation, it seems that, in order to have TBA binding, the TNA must first be

bound by a PNA (probe nucleic acid). This is confusing regarding the practice of instant claims 28, 29, and 49 because there is no administration of a PNA to the patient (claims 28 and 29) or PNA introduction into a cell (claim 49) such that a TBR (TNA-PNA hybrid) may be firstly formed in order to permit binding of the hybrid to the TBA. Rather, only a TBA seems to be administered to the patient or the cell in these instant claims. Given the above noted page 5 definition of a TBA, claims 28, 29, and 49 seem to lack a required PNA presence in the patient or cell. In the specification on pages 12-13, definitions are given for various entities. On page 12, lines 33-34, a TBA may typically bind "DNA sequences" which are uncharacterized as to being single or double stranded. On page 13, lines 1-2, a TBA may bind to RNA sequences, such as antisense polynucleotides. It is noted that RNA may be either single or double stranded but are most commonly characterized as being single-stranded. Then on page 13, lines 4-12, the basis of TBA discrimination is stated as being directed to the formation of PNA-TNA hybrids of various types. In summary, it is unclear whether TBA are required to bind only to PNA-TNA hybrids or whether TBAs also may recognize and bind single stranded forms of nucleic acid, such as RNAs. Both interpretations may be reasonable, given the above noted citations. Clarification via clearer claim wording is requested.

Claim 49 is also vague and indefinite as to what actually is meant to be introduced into a cell in the claimed method. In claim 49, line 2, "component TBAs" are introduced into a cell. This is reasonably interpreted as being introduction of TBAs per se through a cell's membrane and into a cell. In claim 49, line 8, the TBAs are characterized as "expressed TBAs". Expression suggests that the TBAs per se are produced via expression activity within a cell and are not originally present in the cell prior to said expression. A vector or plasmid, for example, may be inserted into a cell in order to be subject to enzyme activity within the cell which expresses a TBA which is encoded by said vector or plasmid. These two interpretations conflict. Clarification is requested via clearer claim wording.

Claim 49 is additionally vague and indefinite as to the practice of the past tense phrase "expressed TBAs" in the last line. The wording "expressed" indicates a past performance of expression. This raises the question as to whether the actual performance of expression of the TBAs in the claim is prior to the claimed steps or not. That is, if a method cites the usage of TBAs but without describing their expression within a method, is such a method outside of the practice of instant claim 49? Alternatively, are methods which practice claim 49 required to clearly describe a step of expression of TBAs corresponding to the last line of claim 49? Clarification via clearer claim

wording is requested.

Claim 29 is vague and indefinite as to the antecedent basis for the "said TBA" and the listed sequences in claim 28 from which it depends. In claim 28 the TBA seems to be either a purified protein complex or a recombinant vector which expresses a TBA. It is noted that all of the sequences in claim 29 are amino acid sequences. It is not clear what protein complex might be meant. If an expressed TBA is meant then it is expected that an expressed sequence must start with a Methionine as required for expression. It is noted that SEQ ID NOs: 109-113 all lack a starting Met amino acid. It is thus confusing as to what expressed TBA is meant regarding these sequences because of this lack of a required starting Met amino acid. Clarification is requested as to what TBA is meant regarding SEQ ID NOs: 109-113.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 28 is rejected under 35 U.S.C. § 102(e) as being anticipated by either of Roth et al.(P/N 6,017,524) or Gruber et

al.(P/N 5,830,458).

The abstract of Roth et al. summarizes the invention therein as being directed to manipulation of gene expression via retroviral expression vectors for expressing antisense sequences or encoding a product such as p53. The action of the antisense sequences is summarized in column 4, line 66, through column 9, line 3, wherein particularly, in column 6, lines 47-53, the practice of the invention clearly indicates a nucleic acid which encodes antisense RNA molecules. In column 5, lines 1-9, the encoded RNA is described as being complementary to and binding to target RNA and thus preventing translation. The retroviral delivery constructs are given to patients as summarized in column 7, lines 2-15, and column 14, line 16, through column 15, line 25. Thus the reference describes a TBA of the instant invention which comprises a nucleic acid recognition unit which is complementary, which is well known to be a recognition mechanism for antisense binding to its target. The reference describes the administration of a retroviral vector which encodes the antisense RNA. Thus, the antisense RNA must be expressed as the instant TBA is expressed in instant claim 28. The expressed antisense TBA then exerts a therapeutic effect in patients as also summarized above and required in instant claim 28. Thus, the antisense methods of the reference anticipate the practice of instant claim 28.

In the abstract Gruber et al. also describes the practice of recombinant retroviruses for delivering a vector construct for disease inhibition etc. These vectors are described in column 4, lines 34-58, as exerting their effects via encoding antisense RNA, ribozymes, tumor suppressor genes, etc. The treatment of patients with these constructs is indicated, for example, in column 3, lines 26-32, via disease treatment descriptions therein. Thus, this reference discloses nucleic acid targeted TBA treatments which anticipate instant claim 28 similar to the above reference by Roth et al.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered

therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claim 28 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Frankel et al.(P/N 5,674,980).

In the abstract Frankel et al. discloses the delivery of polypeptides and nucleic acids in vivo intracellularly to cells. In column 18, line 31, through column 19, line 20, a fusion protein of tat and E2 is described as being produced. This fusion protein (a protein complex as in instant claim 28) was tested for animal cell uptake as given in column 18, lines 59-61. Transactivation which is a gene regulatory effect is assessed as given in column 18, lines 62-65, thus indicating a nucleic acid recognition and binding step. In column 6, lines 32-45, the invention therein is summarized as being a method of delivery of proteins etc. into a cell's nucleus which clearly include regulatory factors etc. The practice of such regulatory factors suggests and motivates nucleic acid recognition and therapy thereby. This is discussed more in column 7, lines 6-28, and column 10, lines 39-61, as being directed to living animal or human therapy or prophylactic usage.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the protein complex patient treatments of Frankel et al. wherein

regulation of gene expression is suggested and motivated thus resulting in the practice of this embodiment of instant claim 28.

Claim 49 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Essigmann et al.(P/N 5,882,941).

In the abstract Essigmann et al. disclose agents that inflict damage on cellular DNA. Cells are targeted for treatment as given in column 5, line 39, through column 6, line 5. The TBAs of the reference contain a first and second agent. The first agent binds to genomes and inflict lesions as given in column 7, lines 41-55, and the second agent then, being optionally linked to the first agent, is a multimeric TBA which acts at the lesion. A variety of first agents and their effects are listed in column 8, line 10, through column 10, line 55. The second agent may be linked intracellularly to the first agent as described in column 21, lines 55-63. Thus, multimeric forms are described as being assembled as also required in instant claim 49, last 3 lines.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the first and second agent invention option of Essigmann et al. wherein intracellular assembly of the TBA occurs as a specie thus resulting in the practice of the instant invention. It is noted that a specie within a generic disclosure is deemed suggested and motivated therein as being obvious under 35 U.S.C. § 103(a).

The disclosure is objected to because of the following informalities:

The specification contains a section entitled "Brief Description of the Drawings" starting on page 7. These Brief Descriptions are confusing regarding a lack of correspondence between the capitalization or not of designations of Figures and subparts thereof. For example, on page 7, line 25, the designation "Figure 1-IIa" is given but consideration of Figure 1 revealed that there is a subpart IIA but no subpart IIa. On page 7, lines 26-34, similar differences in capitalization or not between the Figures and the Brief descriptions exists and is confusing. Additionally, on page 8, lines 10 and 12, Figures 2a and 2b, respectively, are described. Consideration of the actual Figures revealed that Figures 2A and 2B are present but not Figures 2a and 2b. Applicants are requested to review all of the Brief Figure Descriptions in the specification versus the actual Figures and remove capitalization differences. It is noted that these conflicts also are present in numerous locations elsewhere in the specification. For example, at page 10, line 8, a Figure 5(Ia) is cited but confusingly is Figure 5(IA) in the actual Figure. Also, on page 37, line 26, Figures 12a and 12b are cited but confusingly there are only Figures 12A and 12B.

Appropriate correction is required.

No claim is allowed.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to the Technical Center receptionist whose telephone number is (703) 308-0196.

August 8, 2000

Ardin H. Marschel

ARDIN H. MARSCHEL
PRIMARY EXAMINER